UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/749,419	12/31/2003	Young-A Kim	YPL-0071	9573

23413 7590 04/27/2006

CANTOR COLBURN, LLP
55 GRIFFIN ROAD SOUTH
BLOOMFIELD, CT 06002

EXAMINER	
BABIC, CHRISTOPHER M	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/749,419	KIM ET AL.	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 12-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 December 2004 and 6 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-10 and 12-21 are pending. The following Office Action is in response to Applicant's response dated February 14, 2006.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-2 and 5-8 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cantor et al (U.S. 5,795,714) in view of Koster et al. (U.S. 6,133,436).

Regarding claim 1, Cantor et al teach a method of replicating a nucleic acid array, the method comprising: (a) manufacturing a template nucleic acid array by immobilizing on a surface of a first substrate first nucleic acid probes (claim 1., column 53, lines 28-33), each of which includes a first polynucleotide that has a sequence complementary to a second polynucleotide to be synthesized and a primer binding site.

Due to the inherent nature of polynucleotides, a first polynucleotide will have a second polynucleotide to which it will be complementary. Any sequence contained within the first nucleotide to which a polynucleotide complementary to said first nucleotide might bind may be interpreted as a primer binding site. (b) binding a primer to the primer binding site of each of the first nucleic acid probes immobilized on the surface of the first substrate of the template nucleic acid array (claim 1; column 53, lines 34-36)., (c) in-situ synthesizing a second polynucleotide initiating from the primer using the first polynucleotide as a template (claim 1; column 53, lines 37-38)., and (d) transferring second nucleic acid probes, each of which includes the second polynucleotide and the primer, to a second substrate from the first substrate (claim 1 ; column 53, lines 40-43).

Furthermore, Cantor et al. teach a master array consisting of a set of streptavidin bead-impregnated plastic coated metal pins (i.e. protruding portion), each of which, at its tip, contains immobilized biotinylated DNA strands (Column 21, Lines 59-63). They teach incubating the master array with 5'-biotinylated complements of the DNA probes and synthesizing the complement with polymerase (Column 21, Lines 64-65). They teach the transfer of the newly synthesized 5'-biotinylated from the master array to the streptavidin-coated replica surface (Column 22, Lines 1-3). They further highlight that the advantage of this scheme is that the master (i.e. template) array is made only once and allows replication to continue endlessly (Column 22, Lines 10-15).

Cantor et al. do not specifically disclose the manufacturing of the *template* (i.e. master) array by bringing the streptavidin bead-impregnated plastic coated metal pins

(i.e. protruding portion) into a solution of biotinylated DNA strands located in a recessed portion of another uneven substrate (e.g. well, concave cavity).

Koster et al. disclose a pin-tool in a 4x4 array (Figure 8) wherein nucleic acid can be directly captured onto the pin-tool, for example, a linking functionality on the pin-tool (e.g. streptavidin) can *immobilize* the nucleic acid upon contact (Column 8, Lines 6-8). They further disclose that immobilization can result from application to the pin-tool of an electric field (Column 8, Lines 8-10). Figure 14 clearly shows a pin (i.e. protruding portion) coming into contact with a solution of nucleic acid contained in a recessed portion of another substrate (e.g. concave cavity) in order to *immobilize* the nucleic acid onto the pin.

Based on the combined disclosures of Cantor et al. and Koster et al., one of ordinary skill in the art at the time of invention would have had a reasonable expectation of success practicing a method of replicating a nucleic acid array by the methods of Cantor et al. further comprising bringing the streptavidin bead-impregnated plastic coated metal pins (i.e. protruding portion) into a solution of biotinylated DNA strands located in a recessed portion of another uneven substrate (e.g. concave cavity) in order to immobilize the template array. The disclosure of Koster et al. clearly would have provided the instruction necessary for one of ordinary skill in the art at the time of invention to immobilize a nucleic acid array on a protruding substrate by bringing it into contact with a solution of nucleic acid contained in a recessed portion of another substrate (e.g. concave cavity). The motivation to manufacture the template array for use in the methods of Cantor et al. would have been to create a master array, through a

one-time procedure, for continuous manufacture of replica arrays. It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to practice the methods as claimed.

Regarding claim 2, Cantor et al teach the first and second substrates are previously surface-treated, i.e. coating the surface (column 15, lines 23-28).

Regarding claim 5 and 12, Cantor et al teach the use of universal primers, i.e., the complement of the common region (column 4, lines 26-29; column 4, lines 48-61; column 33, lines 44-46).

Regarding claim 6, Cantor et al teach attaching to a terminal of the primer one of a functional group and a material that can bind to a surface of the second substrate, e.g. streptavidin/biotin (column 15, lines 23-28).

Regarding claim 7, double-stranded DNA is held together via hydrogen bonding. Cantor et al teach denaturation of double stranded nucleic acids (column 53, line 40) and therefore teach cleaving hydrogen bonds between the first and second polynucleotides before step (d).

Regarding claim 8, Cantor et al teach repeated use of the template nucleic acid array to produce a number of nucleic acid arrays (column 14, lines 5-8).

2. Claims 3-4, 9-10, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cantor et al (U.S. 5,795,714) in view of Koster et al. (U.S. 6,133,436), in further view of Dickinson et al (U.S. 6,770,441).

Regarding claims 3 and 9-10, and 13 the methods of Cantor et al. and Koster et al. have been outlines in the above rejection. Neither Cantor et al. or Koster et al. specifically disclose a metallic pattern formed on the substrates. Dickinson et al teach the first and second substrates are previously patterned or surface-treated, i.e. metal-coated for the advantage of enhanced signal collection from the arrays (column 10, lines 18-20).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of Dickinson et al and Cantor et al to fabricate a nucleic acid array with a metallic pattern on the substrate for the advantage of "enhanced signal collection from the arrays" (Dickinson et al, column 10, lines 18-20). Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made.

Regarding claim 4, Cantor et al teach the use of streptavidin/biotin (column 15, lines 23-28).

With specific regard to the amendments of Claim 13, Koster clearly suggests substrates with metallic patterns.

Furthermore, Koster discloses thiolated DNA as a means for attaching nucleic acids to solid supports. It would have been *prima facie* obvious to a practitioner of ordinary skill in the art at the time of invention to incorporate thiol groups into nucleic acid probes since Koster suggests such a modification for the purposes of DNA immobilization.

With regard to Claim 18, Cantor teaches the use of universal primers, i.e., the complement of the common region (Column 21, Lines 55-65, for example).

With regard to Claim 19, Cantor teaches attaching to a terminal of the primer one of a functional group and a material that can bind to a surface of the second substrate, e.g. streptavidin/biotin (column 15, lines 23-28, for example)

With regard to Claim 20, Cantor discloses primers with a terminal biotin label (Column 21, Lines 60-67, for example).

With regard to Claim 21, please refer to the rejection of Claim 13.

3. Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cantor et al (U.S. 5,795,714) in view of Koster et al. (U.S. 6,133,436), in further view of Dickinson et al (U.S. 6,70,441), in further view of Yan et al. (U.S. 5,830,539).

Regarding Claims 14 and 15, the methods of the previously applied references above have been outlined in the above rejections. None of the previously applied references expressly disclose a substrate comprising a platinum metallic pattern.

Yan et al. expressly discloses a method for immobilizing nucleic acids on platinum substrates (Column 51, Examples 46 and 47). As outlined above, Dickinson teaches substrates previously patterned or surface-treated, i.e. metal-coated for the advantage of enhanced signal collection from the arrays (column 10, lines 18-20).

It would have been *prima facie* obvious to a practitioner of ordinary skill in the art at the time of invention to incorporate a platinum coated substrate into the methods of Cantor and Koster since Yan and Dickson suggest such a modification for the purposes of DNA immobilization and enhanced signal collection from the arrays.

4. Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cantor et al (U.S. 5,795,714) in view of Koster et al. (U.S. 6,133,436), in further view of Dickinson et al (U.S. 6,70,441), in further view of Nikiforov et al. (U.S. 5,610,287).

Regarding Claims 15 and 16, the methods of the previously applied references above have been outlined in the above rejections. None of the previously applied references expressly disclose forming patterns on substrates through photolithography.

Nikiforov et al. expressly disclose patterning of substrates through photolithography for the purposes masking areas of substrates to prevent oligonucleotide binding.

It would have been *prima facie* obvious to a practitioner of ordinary skill in the art at the time of invention to incorporate patterning of substrates through photolithography into the methods of Cantor, Koster, and Dickson since Nikiforov suggest such a modification for the purposes masking areas of substrates to prevent oligonucleotide binding.

Response to Arguments - Claim Rejections - 35 USC § 103

Applicants' arguments with respect to the rejections of Claims 1-13 have been fully considered but they are not persuasive.

Applicants argue that they can find no teaching or suggestion in Koster to use the 4 x 4 pin-tool as a substrate for a template nucleic acid array, or to use the pin-tool to inhibit mixing of different nucleic acids to be captured among themselves. Thus, it would not be obvious to one of ordinary skill in the art to introduce the pin-tool apparatus disclosed in Koster into the manufacturing of the template array disclosed by Cantor for the purpose of inhibiting differing first nucleic acid probes. First, it was not suggested to incorporate the pin-tool disclosed by Koster into the methods of Cantor as Cantor already discloses a pin-tool. The Koster reference is relied upon merely to suggest the immobilization of a nucleic acid in the manner disclosed in the instant claims. The Cantor reference teaches the overwhelming majority of the limitations set forth in the Claim 1, however, does not necessarily infer the immobilization limitation with regard to the master array. The disclosure of Koster et al. clearly would have provided the suggestion necessary for one of ordinary skill in the art at the time of invention to immobilize a nucleic acid array on a protruding substrate by bringing it into contact with a solution of nucleic acid contained in a recessed portion of another substrate (e.g. concave cavity). In addition, Applicant's arguments with respect to the use of the pin-tool to inhibit mixing of different nucleic acids to be captured among themselves are moot as they are not commensurate in scope with the current claims.

However, Koster clearly suggests reaction wells that inhibit mixing of nucleic acids (Column 7, Lines 50-65, for example).

Applicants further argue that they can find no teaching or suggestion of a first and second substrate that are previously patterned or surface-treated in the disclosure of Dickson. First, Dickson is not relied upon to demonstrate first and second substrates that are previously patterned or surface-treated. Cantor teaches the first and second substrates as previously surface-treated, i.e. coating the surface (Column 15, Lines 23-28; Column 21, Lines 55-65, for example). With specific regard to Claim 13, absent of any specific definition of the term "pattern" and its other forms, this term can be examined under its broadest reasonable interpretation. As Applicants highlight, Dickson clearly teaches metal-coated substrates to enhance signal collection. A coat of metal can be interpreted as a solid "pattern." Please refer to the above rejections for discussion of the teaching of a terminal thiol group.

As such, the rejections are maintained.

Conclusion

Claims 1-10 and 12-21 are rejected. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

4/17/06

Christopher M. Babic
Patent Examiner
AU 1637

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

4/25/06